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Case Report

Polycythemia Vera Associated with Diffuse Large B-Cell Lymphoma: A Case Report

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Abstract

Diffuse Large B-cell Lymphoma (DLBCL) is the most common type of non-Hodgkin's lymphoma, accounting for more than 30% of cases, particularly in developing countries. Polycythemia Vera (PV) is a chronic myeloproliferative disorder characterized by an increase in the number of red blood cells, and often leukocytes and peripheral blood platelets. PV is most commonly diagnosed in individuals around the age of 60, and slightly more common in women, the clinical course is long and can lead to thrombotic complications, which may be the first symptom of the disease. In approximately 10% of patients, PV may progress to Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML).

The co-occurrence of DLBCL with a JAK2V617F-positive Myeloproliferative Neoplasm (MPN) is rarely documented in the literature. Here we describe a 64-year-old patient diagnosed with both DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) and polycythemia, with a particularly short time between identification of these conditions.

Introduction

Polycythemia Vera (PV) is a rare hematological disorder that belongs to the category of Myeloproliferative Neoplasms (MPNs). The condition is characterized by the overproduction of red blood cells, white blood cells, and platelets in the bone marrow. It is caused by a genetic mutation that leads to the activation of the JAK2 kinase pathway, resulting in the proliferation of hematopoietic stem cells. The most common mutation associated with PV is the JAK2V617F mutation, which is present in over 95% of patients [1]. Accounting for 30% of non-Hodgkin's lymphoma cases, diffuse large B-cell lymphoma (DLBCL) is the most prevalent type of this malignancy [2]. The exact cause of DLBCL is not known, but it is thought to arise from genetic mutations that disrupt the normal regulation of B-cell growth and survival [3]. The coexistence of PV and DLBCL is a rare occurrence, and the exact mechanism underlying this association is not fully understood. However, it has been suggested that chronic inflammation and the activation of the JAK2 kinase pathway may play a role in the development of DLBCL in patients with PV [4]. Several case reports have documented the co-occurrence of PV and DLBCL [5-7]. However, due to the rarity of this event, there are no large-scale studies that have investigated the incidence and prevalence of this association. Therefore, the management of patients with both PV and DLBCL remains challenging, and the optimal treatment approach has not been clearly defined [8].

Case Presentation

A 64-year-old male patient was referred to the Hematology Department of Avicenne University Hospital in Rabat, Morocco, in March 2021 for suspected polycythemia vera. Blood morphology showed an Hb concentration of 20.3g/dl, Ht of 58%, WBC of 10G/L, and PLT of 254G/L. FISH testing revealed the presence of the V617F mutation in the JAK-2 gene, and no BCR/ABL fusion was detected.

Histopathological examination of the bone biopsy confirmed the diagnosis of PV. Abdominal ultrasound showed significant splenomegaly (spleen size 210x140mm). The only symptom reported by the patient was night sweats. Treatment with hydroxycarbamide and low-dose aspirin was initiated, and blood was frequently drained. From April 2022 onwards, a progressive increase in cervical and supra- clavicular lymph nodes, and right hepatosplenomegaly were observed. The patient continued to complain of night sweats. A neck lymph node biopsy was performed, and based on histopathological examination, the diagnosis of DLBCL was made with a CD20 (+), BCL-2 (+), CD5 (+), CD23 (-), MUM1 (-), CD3 (-), CD10 (-), CD21 (-), SOX11(-), CyclinD1 (-), BCL-6 (-) immunophenotype. A CT scan of the thorax revealed a 40x55 mm lymph node bundle in the right supraclavicular region with a left lateralized oropharyngeal process and associated lymph node changes extending along the anterior mediastinum to a length of 110mm. An abdominal CT

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scan showed an enlarged liver (about 200mm on the midclavicular line), splenomegaly (210x65x180 mm), and lymph nodes up to 45mm in diameter in the retroperitoneal space. On a PET scan, there was pathological left oropharyngeal hypermetabolism associated with abdominal supra- and sub-diaphragmatic lymph node hypermetabolism, hepatic hilum, and the small curvature of the stomach. Histopathological examination of the bone biopsy showed no lymphomatous infiltration, and the bone marrow picture was still compatible with the diagnosis of polycythemia. On follow-up laboratory examinations, increased lactate dehydrogenase (LDH-483U/L; normal range: 125-220) and β2-microglobulin (3.5mg/L; normal range: 1.1-2.4mg/L) were noted. The morphologic picture of the blood was normal. Clinical stage was determined as IV according to the Ann Arbor classification, IPI-4. First-line treatment used the R-CHOP-21 regimen (Rituximab- Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisolone). After four courses of chemotherapy, regression of the tumor syndrome with a decrease in size and number of mediastinal ADPs and disappearance of cervical ADPs, the patient continued his treatment with 2 other courses according to the R-CHOP protocol with a complete response at the end of the treatment.

Discussion

Polycythemia Vera (PV) is a chronic myeloproliferative neoplasm characterized by the overproduction of red blood cells, while Diffuse Large B-Cell Lymphoma (DLBCL) is a type of non-Hodgkin's lymphoma that develops from B cells. The association between these two diseases is rare, and the underlying pathophysiology is unknown. PV is diagnosed through a combination of medical history, physical examination, and laboratory tests, including blood tests, gene testing, and bone marrow biopsy. DLBCL is diagnosed through a biopsy of the affected tissue. PV is a chronic disease that is not curable, but it can usually be managed effectively for many years with careful medical supervision. Treatment goals are aimed at symptom relief and reducing the risk of disease complications [8-10].

The co-occurrence of Polycythemia Vera (PV) and Diffuse Large B-Cell Lymphoma (DLBCL) is rare, and the underlying pathophysiology of this association is not yet fully understood. However, a few cases have been reported in the literature and recent studies suggest that the JAK2V617F mutation may contribute to the development of PV and DLBCL. The JAK2V617F mutation is the most common genetic defect in PV, present in approximately 95% of cases [11-12]. This mutation results in constitutive activation of the JAK-STAT signaling pathway, resulting in uncontrolled cell proliferation and survival. Similarly, the JAK-STAT pathway is also activated in some types of lymphoma, including DLBCL. It is therefore possible that the JAK2V617F mutation plays a role in the pathogenesis of PV and DLBCL. The diagnosis of PV in patients with DLBCL can be difficult [11,13,14], as both conditions can present with similar symptoms such as fever, night sweats and weight loss. However, bone marrow biopsy and JAK2V617F mutation analysis should be performed in patients with unexplained leukocytosis, thrombocytosis, or erythrocytosis to distinguish the two conditions. In the case discussed, the patient's initial presentation with fever, night sweats, and weight loss was likely due to his underlying DLBCL rather than his history of PV. The JAK2V617F mutation, common in PV, may have contributed to the development of DLBCL in this patient. Treatment of PV in patients with DLBCL requires a multidisciplinary approach. PV can be treated with phlebotomy, low-dose aspirin, and cytoreductive hydroxyurea therapy. On the other hand, DLBCL is usually treated with chemotherapy, rituximab, and radiation therapy. However, the use of cytotoxic chemotherapy in patients with PV requires special attention because it may exacerbate myeloproliferative disorders. Therefore, treatment plans should be individualized based on the patient's clinical presentation and underlying medical history.

Conclusions

Although the association between PV and DLBCL is rare, it is important to consider this possibility in patients with unexplained leukocytosis, thrombocytosis or erythrocytosis. Analysis of the JAK2V617F mutation may be helpful in distinguishing the two conditions. Treatment requires a multidisciplinary approach and must be tailored to the needs of each patient. Further studies are needed to fully understand the underlying pathophysiology of this association and to identify potential therapeutic targets.

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